REMARKS

This amendment responds to the Office Action mailed November 6, 2002. Claims 1, 4, 8, 55 and 57 were pending in the instant Application. With the instant amendment, Applicants have canceled Claims 1, 4, 8, 55 and 57, without prejudice, and added new Claims 112-116. Support for new Claims 112-116 can be found in the specification and the claims as originally filed. Support for new Claim 112 can be found, for example, at page 18, lines 3-25, and Claim 1 as originally filed. Support for new Claim 113 can be found, for example, at page 18, lines 3-25, and Claim 4 as originally filed. Support for new Claim 114 can be found, for example, at page 18, lines 3-25, and Claim 8 as originally filed. Support for new Claim 115 can be found, for example, at page 18, lines 3-25, and Claim 55 as originally filed. Support for new Claim 116 can be found, for example, at page 18, lines 3-25, and Claim 57 as originally filed.

After entry of this amendment, Claims 112-116 will be pending. Applicants expressly reserve the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

I. THE REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 4, 8, 55 and 57 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled. As pointed out, above, none of Claims 1, 4, 8, 55 or 57 are currently pending. However, for the reasons set forth below, Applicants assert that the pending claims are fully enabled under 35 U.S.C. §112, first paragraph.

The PTO bases its rejection of Claims 1, 4, 8, 55 and 57 on the contention that "it is not clear from the claims if the levels of expression of the indicator gene being measured and compared are levels of expression of the indicator gene as in the same host cell, and whether the expression of the indicator gene is dependent on the patient-derived segment comprising a HCV gene." (Office Action, p. 3). Specifically, the claims are rejected because the PTO contends that it is not known what effect using different types of host cells or using indicator genes whose expression is not dependent upon a patient-derived patient segment would be.

New Claims 112-116 are fully enabled by the specification as originally filed and merely clarify that which Applicants have always considered the claimed subject matter. In particular, in the methods recited in each of the claims indicator gene expression is dependent upon the patient-derived segments. In each of the claims where more than one set of host

cells is being compared (*i.e.*, Claims 112-114 and 116), indicator gene expression is measured in corresponding, not different, host cells. As such, neither of the above-summarized concerns with respect to Claims 1, 4, 8, 55 or 57 is relevant to the enablement of the subject matter recited in the pending claims.

II. THE REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

A. The Rejection of Claims 1, 4, 8, 55 and 57

Claims 1, 4, 8, 55 and 57 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As pointed out, above, none of Claims 1, 4, 8, 55 or 57 are currently pending. However, for the reasons set forth below, Applicants assert that the pending claims are definite under 35 U.S.C. §112, second paragraph.

The PTO bases its rejection of Claims 1, 4, 8, 55 and 57 on the contention that step (c) of Claim 1 is unclear. (Office Action, p. 3). Specifically, the claims are rejected because the PTO contends that "[i]t is unclear . . . if the expression of the indicator gene being compared with the expression measured in step (b) is a comparison of the indicator gene expression while in the same cell or in another cell." (Office Action, p. 4). The PTO further contends that "it is unclear if the reference to (a) is an identification of indicator gene alone or an indication that step (a) is being repeated except that the cell is being cultured in the absence of the anti-viral drug." *Id.*

New Claims 112-116 are definite and particularly point out that which Applicants have always considered the claimed subject matter. In particular, in each of the claims where more than one set of host cells is being compared (*i.e.*, Claims 112-114 and 116), indicator gene expression is measured in corresponding host cells, that is, host cells of the same type. Further, Claims 112-114 clearly state that the indicator gene expression is measured in corresponding host cells in the presence and in the absence of the HCV anti-viral drug are compared As such, neither of the above-summarized concerns with respect to Claims 1, 4, 8, 55 or 57 is relevant to the definiteness of the pending claims.

B. The Rejection of Claims 55 and 57

Claims 55 and 57 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As pointed out, above, neither Claim 55 nor Claim 57 are currently

pending. However, for the reasons set forth below, Applicants assert that the pending claims are definite under 35 U.S.C. §112, second paragraph.

The PTO bases its rejection of Claims 55 and 57 on the contention that "it is unclear from the claims if the methods are being conducted *in vitro* or *in vivo*. (Office Action, p. 4). Specifically, the claims are rejected because the PTO contends that Claims 55 and 57 recite the determination of drug resistance "in a patient" indicating that the method is being carried out *in vivo*, but, at the same time, depend from Claim 1, which is an *in vitro* test. *Id.* The PTO further contends that that the reference in Claims 55 and 57 to the method of Claim 1 is unclear. *Id.*

The pending claims are definite and particularly point out that which Applicants have always considered the claimed subject matter. In particular, while indeed, the methods are directed to determining resistance or susceptibility of a patient's viral population of HCV to an anti-HCV drug, each of the claims makes clear that the steps of the method utilize cells in culture.

III. THE REJECTIONS UNDER 35 U.S.C. § 102(e)/103(a) SHOULD BE WITHDRAWN

Claims 1, 4, 8 and 57 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over Rice *et al.*, 2000, U.S. Patent No. 6,127,116 ("Rice"). As pointed out, above, none of Claims 1, 4, 8 or 57 are currently pending. However, for the reasons set forth below, Applicants assert that the pending claims are not anticipated by, nor rendered obvious in view of, Rice.

New Claims 112-116 reflect that which Applicants have always considered the claimed subject matter. They clarify that the methods are directed to determining susceptibility or resistance of a HCV viral *population* in a patient for an HCV anti-viral drug. Nowhere in Rice are the methods of Claims 112-116 taught, nor do any teachings of Rice suggest methods for determining susceptibility of a HCV viral *population* in a patient for an HCV anti-viral drug. Rice, at best, proposes that *individual* sequences might be identified that are resistant to anti-HCV therapy such that the molecular and structural basis of that resistance can be determined and new drugs developed (see Rice, Column 38, lines 20-26). This in no way teaches or suggests the assays recited in the pending claims.

Accordingly, Rice does not anticipate, and cannot render obvious, the methods of Claims 112-116.

IV. THE REJECTIONS UNDER THE DOCTRINE OF OBVIOUSNESS-TYPE DOUBLE PATENTING SHOULD BE HELD IN ABEYANCE

Claims 1, 4, 8, 55 and 57 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1, 4, 7-11, 13, 14, 46-49, 51-53, 70-73 and 78-83 of U.S. Patent No. 5,837,464, in view of Lu *et al.*, and Wang *et al.*, or over Claims 1, 2, 18, 24-27 and 30-42 of U.S. Patent No. 6,242,187, in view of Lu *et al.*, and Wang *et al.* Applicants respectfully request that this rejection be held in abeyance until this is the final outstanding issue.

CONCLUSION

Applicants respectfully submit that Claims 112-116 satisfy all the criteria for patentability and are in condition for allowance. Applicants request that the Examiner reconsider this application with a view towards allowance and solicit an early passage of Claims 112-116 to issuance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is hereby authorized to charge all required fees, including fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds, LLP U.S. Deposit Account No. 16-1150 (order no. 011068-043-999).

Respectfully submitted,

Date: May 6, 2003

Nikolaos C. George 39,201
Nikolaos C. George (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, NY 10036-2711
(212) 790-9090